

The following listing of claims will replace all prior versions of claims in the application.

**Listing of Claims:**

1. (cancelled).
14. (withdrawn).
15. (withdrawn).
16. (withdrawn).
17. (withdrawn).
18. (cancelled).
19. (cancelled).
20. (withdrawn).
21. (currently amended) A method of producing a transgenic, non-human mammal having integrated into its genome a defined segment of DNA, comprising :
  - a. obtaining a yeast-bacteria shuttle vector comprising a yeast replication origin, a yeast selection marker gene, a bacterial replication origin, a bacterial selection marker gene, at least one unique cloning site, and sequences homologous to sequences flanking the defined segment of DNA, wherein said bacterial replication origin is selected from the group consisting of P1 replicon and F factor origin of replication;
  - b. linearizing the vector within the homologous sequences to form recombinogenic ends;
  - c. introducing the linearized vector into a yeast cell containing DNA comprising the defined segment of DNA, wherein the linearized vector and defined segment of DNA homologously recombine to form a recombinant product;

- d. selecting for the recombinant product;
- e. transferring the recombinant product to bacteria for amplification;
- f. isolating the defined segment of DNA from the recombinant product;
- g. integrating the defined segment of DNA into the genome of a mammal by microinjection of a fertilized egg;
- h. transferring the fertilized egg containing the defined segment of DNA to a pseudopregnant non-human mammal; and
- i. allowing the fertilized egg containing the defined segment of DNA to develop into a transgenic, non-human mammal.

22. (previously added) The method of claim 21, wherein the defined segment of DNA is mutated by yeast genetics.

23. (previously added) The method of claim 21, wherein the defined segment of DNA is mutated in bacteria.

24. (previously added) The method of claim 21, wherein said transgenic mammal is a mouse.

25. (previously added) The method of claim 21, wherein the yeast-bacteria shuttle vector is pCLASPER.

26. (cancelled).

27. (cancelled).

28. (cancelled).

29. (currently amended) A method of producing a transgenic, ~~non-human embryo~~ mouse having integrated into its genome a defined segment of DNA, comprising :

- a. obtaining a yeast-bacteria shuttle vector comprising a yeast replication origin, a yeast selection marker gene, a bacterial replication origin, a bacterial selection marker gene, at least one unique cloning site, and sequences homologous to sequences flanking the defined segment of DNA, wherein said bacterial replication origin is selected from the group consisting of P1 replicon and F factor origin of replication;

- b. linearizing the vector within the homologous sequences to form recombinogenic ends;
- c. introducing the linearized vector into a yeast cell containing DNA comprising the defined segment of DNA, wherein the linearized vector and defined segment of DNA homologously recombine to form a recombinant product;
- d. selecting for the recombinant product;
- e. transferring the recombinant product to bacteria for amplification;
- f. isolating the defined segment of DNA from the recombinant product;
- g. integrating the defined segment of DNA into a specific site in the genome of embryonic stem cells by homologous recombination;
- h. isolating the embryonic stem cells having integrated into their genome the defined segment of DNA;
- i. injecting the embryonic stem cells of step (h) into a blastocyst;
- j. transferring the blastocyst to a pseudopregnant mouse and allowing the blastocyst to develop into a transgenic, chimeric mouse;
- k. identifying the transgenic non-human embryo, chimeric mouse that has integrated into its genome the defined segment of DNA;
- l. breeding the transgenic, chimeric mouse to identify germ-line transmission of the defined segment of DNA; and
- m. breeding the germ-line transmitting offspring to produce a transgenic mouse.

30. (previously added) The method of claim 29, wherein the defined segment of DNA is mutated by yeast genetics.

31. (previously added) The method of claim 29, wherein the defined segment of DNA is mutated in bacteria.

32. (cancelled)..

33. (cancelled).

34. (cancelled).

35. (cancelled).

36. (cancelled).

37. (cancelled).

38 (new) The method of claim 21 further comprising breeding the transgenic, non-human mammal to establish a transgenic, non-human mammalian line.

39. (new) The method of claim 29, wherein the yeast-bacteria shuttle vector is pCLASPER.